I. AMENDMENTS

A. In the Specification

Please amend the specification at page 4, lines 4-8, as follows:

FIGURES 2A AND 2B show the nucleotide (SEQ ID NO:9) and predicted amino acid (SEQ ID NO:10) sequences ~~sequence~~ of GDF-5. The putative tetrabasic processing sites are dented by stippled boxes.

C1

FIGURE 3A shows the alignment of the C-terminal sequences of GDF-5 (SEQ ID NO:13) with other members of the TGF-β family (SEQ ID NOS: 11, 12, and 14 to 27, respectively). The conserved cysteine residues are shaded. Dashes denote gaps introduced in order to maximize alignment.

Please amend the specification at page 25, line 13, to page 26, line 29, as follows (NOTE: underlining of volume number of cited references was in original):

A CD-1 day 12.5 whole mouse embryo cDNA library was constructed in lambda ZAP II and screened with a probe derived from the GDF-5 PCR product. The nucleotide sequence (SEQ ID NO:9) of the longest hybridizing clone is shown in Figure 2. The in-frame termination codons upstream of the putative initiating ATG and the consensus polyadenylation signals are underlined. The poly A tails are not shown. Numbers indicate nucleotide position relative to the 5' end. The 2329 bp sequence (SEQ ID NO:9) contains a long open reading frame (SEQ ID NO:10) beginning with a methionine codon at nucleotide 322 and potentially encoding a protein 495 amino acids in length with a molecular weight of 54.9 K. Like other TGF-β family members, the GDF-5 sequence contains a core of hydrophobic amino acids near the N-terminus suggestive of a signal sequence for secretion. GDF5 contains a single potential N-glycosylation sites at asparagine residue 183 (denoted by the plain box) and two putative tetrabasic proteolytic processing sites at amino acids 371-375 (denoted by the stippled box) and amino acids 384-385 (SEQ ID NO:10). GDF-5 contains all of the highly conserved residues present in other family members (Figures 3 {SEQ ID NOS:11 to 27, respectively} and 4), including the seven cysteine

residues with their characteristic spacing. Among the known mammalian family members, GDF-5 (SEQ ID NO:13) is most highly related to BMP-2 (SEQ ID NO:15) and BMP-4 (SEQ ID NO:16) in the C-terminal portion of the molecule (57% amino acid sequence identity calculated from the first conserved cysteine).

Although the C-terminal portion of GDF-5 clearly shows homology with the other family members, the sequence of GDF-5 is significantly diverged from those of the other family members (Figures 3 {SEQ ID NOS:11 to 27, respectively} and 4). Figure 3 shows the alignment of the C-terminal sequences of GDF-5 with the corresponding regions of human GDF-1 (SEQ ID NO:11; Lee, Proc. Natl. Acad. Sci. USA 88:4250-4254,1991), human Vgr-1 (SEQ ID NO:17; Celeste, et al., Proc. Natl. Acad. Sci. USA 87:9843-9847,1990), human OP-1 (SEQ ID NO:18; Ozkaynak, et al., EMBO J. 9:2085-2093,1990), human BMP-5 (SEQ ID NO:19; Celeste, et al., Proc. Natal. Acad. Sci. USA, 87:9843-9847, 1990), human BMP-3 (SEQ ID NO:20; Wozney, et al., Science, 242:1528-1534, 1988), human MIS (SEQ ID NO:21; Cate, et al. Cell, 45:685-698, 1986), human inhibin α, βA, and βB (SEQ ID NOS:22, 23 and 24, respectively; Mason, et al., Biochem, Biophys. Res. Commun., 135:957-964, 1986), human TGF-β1 (SEQ ID NO:25; Derynck, et al., Nature, 316:701-705, 1985), human TGF-β2 (SEQ ID NO:26; deMartin, et al., EMBO J., 6:36733677, 1987), human TGF-β3 (SEQ ID NO:27; ten Dijke, et al., Proc. Natl. Acad. Sci. USA, 85:4715-4719, 1988), chicken TGF-β4 (Jakowlew, et al., Mol. Endocrinol. 2:1186-1195, 1988), and Xenopus TGF-β5 (Kondaiah, et al., J. Biol. Chem. 265:1089-1093, 1990). The conserved cysteine residues are boxed. Dashes denote gaps introduced in order to maximize the alignment.